Scottish Executive Health Department Chief Scientist Office

FOCUS ON RESEARCH

CLARIFYING THE CAUSES AND CONSEQUENCES OF CHILDHOOD OBESITY

Researchers
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Aim
To try to explain why children appear to become metabolically 'healthier' (falling insulin resistance) between five and eight years of age despite getting fatter (rising adiposity).

Project Outline/Methodology
Insulin resistance is associated with cardiovascular risk factors and predisposes people to diabetes. We are following a cohort of healthy schoolchildren and have found that between 5 and 8 years of age they get fatter but that their insulin resistance falls and their lipids improve. This 'dissociation' between adiposity and insulin resistance is unexpected. We sought to explain it in the current study, by performing serial measurements of four analytes.
We wondered if growth might help to explain it; there is a well established link between growth spurts and insulin resistance, e.g. at puberty. We therefore measured insulin-like growth factor 1 (IGF1), which mediates growth. Separately, we wondered if altered 'adipokines' (substances made/released by fat tissue) might explain it, in particular if the balance between leptin (which marks fatness) and adiponectin (which marks proliferation of new healthy fat cells) changes. Finally we measured C-reactive protein (CRP) as a global marker of cardiovascular risk.

Key Results
(1) Does IGF1 correlate with insulin resistance in healthy children between five and eight years of age. If so, do changes in IGF1 over this period explain why insulin resistance falls?
Yes, IGF1 does correlate with insulin resistance in healthy children between 5y and 8y, although the relationship in boys only emerges clearly at 7y. However, the rise in IGF1 seen over this period does not explain why insulin resistance falls. So this is not the explanation.
(2) Does the leptin/adiponectin ratio fall between 5y and 8y in healthy children in association with improvements in insulin resistance?
No it doesn't; it rises. So adipocyte (fat cell) proliferation does not explain the improved metabolic health of pre-pubertal children between 5y and 8y.
(3) Do changes in CRP, as a marker of cardiovascular risk, have any relationship to changes in insulin resistance in pre-pubertal children?
No, changes in CRP don't have any relationship to changes in insulin resistance in pre-pubertal children.

Conclusions
We have obtained clear answers to each of the three research questions we posed (see previous section). First, fat cell proliferation does not seem to explain the improvement in metabolic health we have seen. Second, rising IGF1 (as a mediator of growth) does not explain it either. Third, there are no clear relationships between CRP and insulin resistance in this cohort of healthy pre-pubertal children.

What does this study add to the field?
We have excluded two plausible explanations for why children become metabolically healthier despite getting fatter between 5y and 8y. By asking clear research questions and getting clear answers, we have advanced the understanding of both the causes and consequences of childhood obesity.

Implications for Practice or Policy
Obesity and the metabolic disturbances it causes are fast becoming a major pre-occupation of the NHS. The value of the current study to the NHS lies in its ability to trace the natural history of insulin resistance and its metabolic correlates throughout childhood. Our data are truly longitudinal and so we are able uniquely to define trends and establish predictions from the age of 5 years onwards.

Where to next?
Having defined clearly the trends in four key metabolic variables in the run-up to puberty, it will now be important to track them through puberty and adolescence where risk of diabetes rises sharply.

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